IN THE SPECIFICATION:

On page 1, paragraph [0001]: This application is a continuation of copending International Patent Application PCT/US02/10850, which was filed on April 8, 2002, which designates the United States of America, which was published under the Patent Cooperation Treaty on October 17, 2002 as Publication Number WO 02/081641, and which (as filed and as published) is incorporated by reference in its entirety herein. This application also claims benefit of priority to Provisional Application Serial no. 60/281,780, filed April 6, 2001, which is incorporated by reference in its entirety herein.

On page 3, paragraph [0007]: Oligonucleotides have been employed as therapeutic moieties in the treatment of disease states in animals and man. For example, workers in the field have now identified antisense, triplex and other oligonucleotide compositions which are capable of modulating expression of genes implicated in viral, fungal and metabolic diseases. ~~tisense~~ Antisense oligonucleotide inhibition of gene expression has proven to be a useful tool in understanding the roles of raf genes. An antisense oligonucleotide complementary to the first six codons of human c-raf has been used to demonstrate that the mitogenic response of T cells to interteukin-2 (IL-2) requires c-raf. Cells treated with the oligonucleotide showed a near-total loss of c-raf protein and a substantial reduction in proliferative response to IL-2. Riedel et al., Eur. J. Immunol. 1993, 23, 3146-3150. Rapp et al. have disclosed expression vectors containing a raf gene in an antisense orientation downstream of a promoter, and methods of inhibiting raf expression by expressing an antisense Raf gene or a mutated Raf gene in a cell. WO application 93/04170. An antisense oligodeoxyribonucleotide complementary to codons 1-6 of murine c-Raf has been used to abolish insulin stimulation of DMA synthesis in the rat hepatoma cell line H4IIE. Tornkvistetal., J. Biol. Chem. 1994, 269, 13919-13921. WO Application 93/06248 discloses methods for identifying an individual at increased risk of developing cancer and for determining a prognosis and proper treatment of patients afflicted with cancer comprising amplifying a region of the c-raf gene and analyzing it for evidence of mutation. Denner et al. discloses antisense polynucleotides hybridizing to the gene for raf, and processes using them. WO 94/15645. Oligonucleotides hybridizing to human and rat raf sequences are disclosed. Iversen et al. discloses heterotypic antisense Oligonucleotides complementary to raf which are able to kill ras-activated cancer cells, and methods of killing raf-activated cancer cells. Numerous oligonucleotide sequences are disclosed, none of which are actually antisense oligonucleotide sequences.

On page 3-4, paragraph [0008]: US Patent No. 5,919,773, to Monia et al. discloses that elimination or reduction of raf gene expression can halt or reverse abnormal cell

proliferation. The Monia et al. patent discloses Oligonucleotides targeted to nucleic acids encoding raf. This relationship between an oligonucleotide and its complementary nucleic acid target to which it hybridizes is commonly referred to as "antisense."

On page 4, paragraph [0010]: in one embodiment, the invention provides an isolated nucleic acid molecule comprising a polynucleotide selected from the group consisting of:

(a) a polynucleotide encoding amino acids from about 1 to about 1297 of the amino acid sequence contained in Figure 1B (SEQ ID NO:2);

(b) a polynucleotide encoding amino acids from about 2 to about 1297 of the amino acid sequence contained in Figure 1B (SEQ ID NO:2);

(c) the polynucleotide complement of the polynucleotide of (a) or (b); and

(d) a polynucleotide at least 90% identical to the polynucleotide of (a), (b) or (c).

On page 4, paragraph [0011]: In another embodiment, the invention provides a method of increasing survival or proliferation of a cell, comprising inhibiting expression of SCC-112 in said mammalian cell. Preferably, the mammalian cell is transformed with a vector encoding an antisense oligonucleotide corresponding to the SCC-112 sequence in Figure 1B (SEQ ID NO:1).

On page 6, paragraph [0019]: (B) cDNA ~~SEQ ID NO 1~~ SEQ ID NO:1 and predicted amino acid sequences ~~SEQ ID NO 2~~ SEQ ID NO:2 of SCC-112. The deduced 6744 bp cDNA sequence of *SCC-112* is shown. Nucleotide positions are indicated by numbers on the *right.* The longest ORF (1297 aa) is shown in single letter code. Amino acid positions are numbered on the *left.* The poly(A)+ signal sequence is shown in a small box at the 3' end. The proposed main structural features of the SCC-112 protein are: RhoGEF domain (2-137 aa, *shaded);* Leucine Zipper pattern (166-187 aa, *underlined);* N-adaptin domain (127-651 aa, *boldfaced),* SKP1 domain (249-350 aa, *not shown here);* three PEST sequence sites (597-617 aa, 1143-1663 aa and 1216-1227 aa, *bolded and underlined)* and two tyrosine kinase phosphorylation sites (858-865 aa and 1030-1036 aa, *shaded and bolded).* Six nuclear localization signature sequences (920-926 aa, 1225-1231 aa, 1227-1230 aa, 1228-1234 aa, 1232-1235 aa, and 1251-1257 aa) are shown as shaded and underlined. SCC-112 ORF reveals some similarities to chromosome associated proteins and cell cycle proteins in other organisms suggesting a possible role of SCC-112 in chromosome rearrangement during cell cycle. N-Adaptin domain is found in vesicle associated proteins such as p-adaptin, 3'-adaptin, (3-NAP and (3-COP involved in protein trafficking. 6-adaptin is a component of AP-2 adapter complex, which is

involved in clathrin- mediated endocytosis in cells. SKP 1 domain has been found in several proteins of SKP1 family (kinetochore protein required for cell cycle progression at both DMA synthesis and mitosis phase and elongin C, subunit of RNA polymerase II transcription factor homologues). SKP1 family proteins have been shown to regulate cell cycle through ubiquitin proteolysis machinery by binding through F-box.

On page 13, paragraph [0040]: The present invention is based at least in part on the identification of a new human gene which has been named by the inventors and as SCC-112. The amino acid sequence of SCC-112 (SEQ ID NO:2) is shown in Figure 1. The invention is also based on the discovery that mRNA expression level of this gene varies during different phases of the cell cycle and is maximum during G phase of the cell cycle (Figure 2). One particular aspect of the invention is based on the discovery that the steady state level of SCC-112 mRNA is relatively higher in androgen-responsive human LNCap prostate cancer cells as compared with hormone-refractory DU-145 and PC-3 prostate cancer cells (Figure 4). This discovery was confirmed through the treatment of LNCap cells with synthetic androgen (R1881 induces SCC-112 mRNA expression in these cells) (Figure 5).

On page 17-18, paragraph [0056]: Sequence identity or percent identity is intended to mean the percentage of same residues between two sequences, wherein the two sequences are aligned using the Clustal method (Higgins et al., Cabios 8:189-191, 1992) of multiple sequence alignment in the Lasergene biocomputing software (DNASTAR, INC, Madison, Wl). In this method, multiple alignments are carried out in a progressive manner, in which larger and larger alignment groups are assembled using similarity scores calculated from a series of pairwise alignments. Optimal sequence alignments are obtained by finding the maximum alignment score, which is the average of all scores between the separate residues in the alignment, determined from a residue weight table representing the probability of a given amino acid change occurring in two related proteins over a given evolutionary interval. Penalties for opening and lengthening gaps in the alignment contribute to the score. The default parameters used with this program are as follows: gap penalty for multiple alignment=IO; gap length penalty for multiple alignment=10; k-tuple value in pairwise alignment=1; gap penalty in pairwise alignment=3; window value in pairwise alignment=5; diagonals saved in pairwise alignment=5. The residue weight table used for the alignment program is PAM25O (~~Dayhoffet~~ Dayhoff et al., in Atlas of Protein Sequence and Structure, Dayhoff, Ed., NDRF, Washington, Vol. 5, suppl. 3, p. 345, 1978).

On page 18, paragraph [0058]: The invention provides polypeptide fragments of the disclosed proteins. Polypeptide fragments of the invention can comprise at least 8, 10, 12, 15, 18, 19, 20, 25, 50, 75, 100, or 108 contiguous amino acids of the amino acid sequence contained in Figure 1B (~~SEQ ID NO 2~~ SEQ ID NO:2). Also included are all intermediate length fragments in this range, such as 51, 52, 53, etc.; 70, 71, 72, etc.; and 100, 101,102, etc., which are exemplary only and not limiting.

On page 19, paragraph [0059]: Variants of the SCC-112 polypeptide disclosed herein can also occur. Variants can be naturally or non-naturally occurring. Naturally occurring variants are found in humans or other species and comprise amino acid sequences which are substantially identical to the amino acid sequence shown in Figure 1B (~~SEQ ID NO 2~~ SEQ ID NO:2). Species homologs of the protein can be obtained using subgenomic polynucleotides of the invention, as described below, to make suitable probes or primers to screening cDNA expression libraries from other species, such as mice, monkeys, yeast, or bacteria, identifying cDNAs which encode homologs of the protein, and expressing the cDNAs as is known in the art.

On page 19, paragraph [0060]: Non-naturally occurring variants which retain substantially the same biological activities as naturally occurring protein variants are also included here. Preferably, naturally or non-naturally occurring variants have amino acid sequences which are at least 85%, 90%, or 95% identical to the amino acid sequence encoded by a nucleic acid sequence comprising the sequence shown in Figure 1B (~~SEQ ID NO 2~~ SEQ ID NO:2). More preferably, the molecules are at least 96%, 97%, 98% or 99% identical. Percent identity is determined using any method known in the art. A non-limiting example is the Smith-Waterman homology search algorithm using an affine gap search with a gap open penalty of 12 and a gap extension penalty of 1. The Smith-Waterman homology search algorithm is taught in Smith and Waterman, *Adv. Appl. Math.* (1981) 2:482-489.

On page 20, paragraph [0063]: It is reasonable to expect that an isolated replacement of a leucine with an isoleucine or valine, an aspartate with a glutamate, a threonine with a serine, or a similar replacement of an amino acid with a structurally related amino acid will not have a major effect on the biological properties of the resulting secreted protein or polypeptide variant. Properties and functions of SCC-112 or polypeptide variants are of the same type as a protein comprising the amino acid sequence encoded by a nucleic acid sequence comprising the nucleotide sequence shown in Figure

1B (~~SEQ ID NO 1~~ SEQ ID NO:1), although the properties and functions of variants can differ in degree.

On page 22, paragraph [0071]: A fusion protein comprises two protein segments fused together by means of a peptide bond. Amino acid sequences for use in fusion proteins of the invention can utilize the amino acid sequence encoded by a nucleic acid sequence comprising the sequence shown in Figure 1B (~~SEQ ID NO 2~~ SEQ ID NO:2) or can be prepared from biologically active variants of Figure 1B (~~SEQ ID NO 2~~ SEQ ID NO:2), such as those described above. The first protein segment can consist of a full-length SCC-112.

On page 22-23, paragraph [0072]: Other first protein segments can consist of at least 8, 10, 12, 15, 18, 19, 20, 25, 50, 75, 100, 108 contiguous amino acids selected from ~~SEQ ID NO 2~~ SEQ ID NO:2. The contiguous amino acids listed herein are not limiting and also include all intermediate lengths such as 20, 21, 22, etc.; 70, 71, 72, etc.

On page 23, paragraph [0074]: These fusions can be made, for example, by covalently linking two protein segments or by standard procedures in the art of molecular biology. Recombinant DNA methods can be used to prepare fusion proteins, for example, by making a DNA construct which comprises a coding sequence comprising the sequence contained in Figure 1B (~~SEQ ID NO 1~~ SEQ ID NO:1) in proper reading frame with a nucleotide encoding the second protein segment and expressing the DNA construct in a host cell, as is known in the art. Many kits for constructing fusion proteins are available from companies that supply research labs with tools for experiments, including, for example, Promega Corporation (Madison, WI), Stratagene (La Jolla, CA), Clontech (Mountain View, CA), Santa Cruz Biotechnology (Santa Cruz, CA), MBL International Corporation (MIC; Watertown, MA), and Quantum Biotechnologies (Montreal, Canada; 1-888-DNA-KITS).

On page 23, paragraph [0075]: Proteins, fusion proteins, or polypeptides of the invention can be produced by recombinant DNA methods. For production of recombinant proteins, fusion proteins, or polypeptides, a coding sequence of the nucleotide sequence shown in Figure 1B (~~SEQ ID NO 1~~ SEQ ID NO:1) can be expressed in prokaryotic or eukaryotic host cells using expression systems known in the art. These expression systems include bacterial, yeast, insect, and mammalian cells.

On page 25, paragraph [0082]: The invention also provides polynucleotide probes which can be used to detect complementary nucleotides sequences, for example, in hybridization protocols such as Northern or Southern blotting or *in situ* hybridizations.

Polynucleotide probes of the invention comprise at least 12, 13, 14, 15, 16, 17, 18, 19, 20, 30, or 40 or more contiguous nucleotides of the sequence contained in Figure 1B (~~SEQ ID NO:1~~ SEQ ID NO:1). Polynucleotide probes of the invention can comprise a detectable label, such as a radioisotopic, fluorescent, enzymatic, or chemiluminescent label.

On page 25, paragraph [0083]: Isolated genes corresponding to the cDNA sequences disclosed herein are also provided. Standard molecular biology methods can be used to isolate the corresponding genes using the cDNA sequences provided herein. These methods include preparation of probes or primers from the nucleotide sequence shown in Figure 1B (~~SEQ ID NO:1~~ SEQ ID NO:1) for use in identifying or amplifying the genes from mammalian, including human, genomic libraries or other sources of human genomic DNA.

On page 28, paragraph [0092]: The targeting sequence is a segment of at least 10, 12, 15, 20, or 50 contiguous nucleotides from the nucleotide sequence shown in Figure 1B (~~SEQ ID NO:1~~ SEQ ID NO:1). The transcription unit is located upstream to a coding sequence of the endogenous gene. The exogenous regulatory sequence directs transcription of the coding sequence of the endogenous gene.

On page 49, paragraph [0166]: **Generation of Anti-SCC-112 Antibody**: A rabbit polyclonal antibody was generated against a peptide representing 20 amino acid reidues (aa) at the C-terminus of the SCC-12 protein (1278-1297, KLQDLAKKAAPAERQIDLQR (SEQ ID NO:3)). This peptide was coupled to keyhole limpet hemocyanin and injected into rabbits. Custom antibody production services of the Zymed Laboratories ~~laboratories~~, Inc., (San Francisco, CA) were used for production of the rabbit anti-SCC-112 antibody.